ACADEMIA ISN'T SO BAD EITHER

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Summary: Drug development follows a very specific path, from preclinical safety and quality ascertainment to clinical development to market authorization and postmarketing surveillance. The whole process is geared to the pharmaceutical industry, which indeed has all the know-how and experience to bring a drug to market, especially when it is also the originator of the future drug. When the product is derived from academic research, can academia initiate drug development, and at what stages? This will depend on the availability of the appropriate resources in the academic and/or private sectors, and the funding for these. Preclinical drug development is not overly expensive, especially for the basic elements needed to pursue drug development and to bring the drug to clinical testing. If the quality issues can be controlled (drug synthesis, stability testing), basic toxicity testing can be outsourced to any of many specialized companies. Obviously, academic laboratories should have all the required resources for pharmacodynamic testing and demonstration. Clinical trials can be done in the appropriate clinical investigation centers, and the academic hospitals of course have all the patients needed for the clinical trials, because this is usually where industry actually does them. Therefore, academia (including public hospitals and research centers) has all the required knowledge and resources needed to develop a drug and bring it to market. What may be most lacking at the premarket phase is financing, and finding this is not easy, especially at the later-phase clinical trials, which are usually multicenter and require heavy logistical resources. Recently developed networks and structures (E-CRIN, F-CRIN) aim to help these large multicenter studies. Increasing awareness by the public research-financing bodies of the need to be able to develop alternatives to industrial development, especially for certain types of drugs (drugs for rare diseases or new uses for old drugs), may also increase the involvement of academia in de novo drug development. Of course, public–private partnerships should continue, both through involvement of industry expertise during academia-initiated development and through the increasingly evident involvement of academia during later-phase clinical development of major new drugs, if only to avoid unnecessary suspicions of industrial misconduct, much as is done in the postmarketing arena with the ENCEPP code of conduct.

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ROLE OF MEMBRANE TRANSPORTERS IN DRUG INTERACTIONS

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Summary: Transporters are membrane proteins, which mediate the translocation of chemicals into and out of cells. The past 10 years have seen an enormous increase in research concerning the role of membrane transporters in drug pharmacokinetics and response.[1] In particular, influx and efflux transporters expressed on the plasma membranes of polarized cells in tissues important for pharmacokinetics have the potential to significantly affect drug response. Certain transporters have been shown to mediate clinically important drug interactions. For example, the immunosuppressive drug cyclosporine increases the systemic exposure to all statins, by ~5- to 20-fold, probably mainly by inhibiting their organic anion transporting polypeptide (OATP)-mediated hepatic uptake.[3] Similarly, cyclosporine raises the systemic exposure to the OATP1B1 substrate antidiabetic repaglinide by 2.5-fold.[2] Furthermore, the P-glycoprotein efflux transporter-inhibiting antimycotic itraconazole raises the systemic exposure to the antihypertensive aliskiren on average 6.5-fold.[4] These and other roles of OATPs, P-glycoprotein. and other membrane transporters in drug interactions will be discussed.

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OVERVIEW OF PHARMACOVIGILANCE IN RESOURCE LIMITED SETTINGS: CHALLENGES AND OPPORTUNITIES

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Summary: Twenty years ago, there were almost no pharmacovigilance (PV) activities in low-and middle-income countries (LMIC). Today, 144 countries are participating in the WHO Programme for International Drug Monitoring, and 102 of them belong to the LMIC category according to the World Bank classification. Many factors have contributed to the positive development. Among them are:

- Creation of evidence of the general burden of drug-related harm in all populations
- Concerns of the high prevalence of substandard and fake medicines in LMIC
- Capacity building and competence development in PV, mainly driven by the WHO Programme
- Public health programs realizing that drug-related harm may jeopardize program success
- Global health initiatives and donor organizations prepared to protect public health programs also by supporting pharmacovigilance

Most of the national pharmacovigilance systems in LMIC still have inadequate capacity to adequately protect their populations from the risk of medicine and medicine use–related harm. There are many challenges that need to be addressed; for example:

- The capacity of National Regulatory Authorities and collaboration and integration with vertical disease programs
- Training of health workers, local industry, and the public about the need to record and report medicine-related harm
- Keeping of systematic patient records
- Documentation of the burden of medicine-related harm in the local setting

In most LMICs, the first requisite for PV activities, the political will, is in place. Further support for the young PV systems is needed to make them fully functional. The WHO Programme builds regional and global networks to support PV in LMIC particularly